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| 10/652,927 | 08/29/2003 | Mark E. Gurney | 29915/6280N3 | 3518 |

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| EXAMINER | |
|---|---|
| EMCH, GREGORY S | |
| ART UNIT | PAPER NUMBER |
| 1649 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/652,927 | GURNEY ET AL. | |
| | Examiner | Art Unit | |
| | Gregory S. Emch | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 April 2007 and 09 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,4,6-11 and 16-19* is/are pending in the application.

4a) Of the above claim(s) *6-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3,4,6-11 and 16-19* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

The replies filed 02 April 2007 and 09 July 2007 have been received and entered in full. Claims 1, 3, 4, 6-11 and 16-19 are pending in the instant application.

Claims 6-11 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in Paper filed on 28 August 2006.

Claims 1, 3, 4 and 16-19 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

This application contains claims 6-11 drawn to an invention nonelected with traverse in Paper filed on 28 August 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The obviousness-type double patenting rejection of claims 1, 3, 4 and 16-19 as being unpatentable over claims 1-7 of U.S. Patent No. 6,913,918 is maintained for reasons of record and as set forth below.

The obviousness-type double patenting rejection of claims 1, 3, 4 and 16-19 as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,825,023 is maintained for reasons of record and as set forth below.

The obviousness-type double patenting rejection of claims 1, 3, 4 and 16-19 as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,828,117 is maintained for reasons of record and as set forth below.

The provisional obviousness-type double patenting rejection of claims 1, 3, 4 and 16-19 as being unpatentable over claims 1-4 of copending Application No. 10/652,830 is maintained for reasons of record and as set forth below.

The provisional obviousness-type double patenting rejection of claims 1, 3, 4 and 16-19 as being unpatentable over claims 151-156 and 159-163 of copending Application No. 10/940,867 is maintained for reasons of record and as set forth below.

In the replies filed 02 April 2007 and 09 July 2007, Applicants request that these double patenting rejections be held in abeyance until there is an indication of allowable subject matter. At that time, Applicants will consider filing appropriate disclaimer(s).

Regardless, until such a time occurs, the rejections are maintained.

### *Claim Rejections - 35 USC § 112, first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The written description rejection of claims 1, 3, 4, 16, 18 and 19 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In the reply filed 02 April 2007, Applicants "request that independent claims 17-19 be examined on their merits rather than be lumped with claim 1...the Examiner's concern as to the structure and activity of the variants is misplaced." Further, Applicants cite several portions of the specification to allegedly support proper written description of the instant claims. Applicants believe that the main basis for rejection appears to be an assertion that the specification does not adequately describe all of the variants embraced by independent claim 1. Applicants also assert that there are only one DTG and one DSG in SEQ ID NO: 4, so the genus of fragments defined by claim 1, part (b) is also well defined by SEQ ID NO: 4." Applicants allege that the combination of limitations used by the Applicants has been recognized by the Patent Office to provide sufficient specificity and limit variability enough to satisfy the written description requirement according to Example 9 of the Patent Office's Written Description Guidelines Training Materials. Applicants assert that claim 16, for example, is adequately described according to Example 9.

Applicants' arguments have been fully considered and are not found persuasive.

First, it is noted that the written description rejection of claim 17 under 35 U.S.C. 112, first paragraph has been withdrawn. Second, contrary to Applicants comment claims 16, 18 and 19 have been examined on the merits and are not simply "lumped" with claim 1. Rather, the claims have been rejected since they encompass fragments and/or variants of SEQ ID NO: 4. Claims 16 and 17 encompass an aspartyl protease containing a valine at a position which corresponds to position 130 of SEQ ID NO: 4 and thus, the only structural requirement recited by the claims is one amino acid residue, i.e., valine. The protease of claim 16 is encoded by "a nucleic acid sequence which hybridizes under stringent wash conditions to a nucleic acid encoding the amino acid sequence set forth in SEQ ID NO: 4" and the protease of claim 18 is encoded by "a nucleic acid sequence which is identical to a sequence set forth in SEQ ID NO: 3." It is noted that the recitation of "stringent wash conditions" is insufficient to provide written description since these conditions are not explicitly claimed or unambiguously defined in the specification. It is also noted that a nucleic acid sequence which is identical to a sequence set forth in SEQ ID NO: 3 encompasses as little as 2 nucleotides of SEQ ID NO: 3. Claim 19 encompasses an aspartyl protease that comprises "an amino acid sequence which is identical across its length to a sequence in SEQ ID NO: 4," and thus, the claimed protein encompasses as little as two amino acids of SEQ ID NO: 4.

Applicants argue that the specification contains an adequate written description of the claimed subject matter because the claims contain a function (aspartyl protease activity) and a structural limitation (a fragment or variant of SEQ ID NO: 4 that contains DTG and DSG). However, in the University of California v. Eli Lilly and Co., 43 USPQ2d

1398 (Fed. Cir. 1997), the court held that one of two elements may satisfy a genus of cDNAS, i.e. a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or; ii) a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.). In the instant case, the first element is not met because only a cDNA encoding SEQ ID NO: 4 is disclosed. The second element requires structural features common to members of the genus. However, in the instant disclosure, insufficient guidance is provided as to which are the critical residues (other than DTG and DSG) that are necessary for the claimed protein function of having aspartyl protease activity.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of

isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Although Applicants assert that the cited passages of the instant specification describe several biologically active truncated forms of the polypeptide of SEQ ID NO: 4, these truncation variants appear to be prophetic and thus, no actual biological function is disclosed for said truncated forms. Further, these prophetic fragments potentially provide support for variants of the full-length polypeptide of SEQ ID NO: 4, not for variants of fragments of the full-length polypeptide (as in claim 1(c)). Applicants point to the Written Description guidelines, which include an example of a claim having written description which is directed to a protein and variants thereof that are at least 95% identical, with a specific catalytic function. Accordingly, the rejected claims are of a larger scope than those deemed adequately described in the Written Description Guidelines.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1, 3, 4 and 19 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,319,689 to Powell et al and as evidenced by Vassar is maintained for reasons of record and as set forth below.

In the reply filed 02 April 2007, Applicants assert that the Powell et al. polypeptide differs from SEQ ID NO: 4 at position 130, which falls within the domain defined by active site tripeptides DTG and DSG. Thus, Applicants assert that Powell et al. does not anticipate claims 1, 3 or 4. In addition, Applicants assert that the genera of polypeptides having conservative substitutions do not include the sequence taught by Powell et al. because the amino acid sequence disclosed in Powell et al. has a Glu at position 130, while SEQ ID NO: 4 has a Val at position 130. Applicants assert that a substitution of Val for Glu is not a conservative substitution, as Glu is an acidic residue and Val is an aliphatic residue and that the amino acid sequence taught in Vassar et al. has a Val at position 130. Applicants allege that the difference in the Powell et al. and Vassar et al. amino acid sequences is within the domain defined by the active site tripeptides. Therefore, Applicants assert that Vassar et al. does not inherently teach an activity for the Powell et al. protein. Applicants also assert, "Powell et al. purports to disclose a deduced amino acid sequence of a protein called Asp2, but Powell et al. fails

to teach or suggest that Powell's Asp2 has a transmembrane domain at all, and certainly does not teach to remove a transmembrane domain for any reason. Likewise, Powell et al. does not by chance teach any specific Asp2 fragment that lacks the region identified by the Applicants as a transmembrane domain of Asp2 in the present application. Thus, Powell et al. does not anticipate the subject matter of claim 4." Applicants further assert that Powell et al. does not anticipate the polypeptide of claim 19, which is identical across its length to "a sequence of SEQ ID NO: 4."

Applicants' arguments have been fully considered and are not found persuasive.

That the Powell et al. patent discloses Glu at position 130 is irrelevant, since the claims do not require that position 130 be valine. The claims require the active site tripeptides of DTG and DSG; the claims do not require any of the residues between these tripeptides. Accordingly, the ASP2 of the Powell et al. reference teaches these active site tripeptides and the patent teaches fragments of the polypeptide that retain aspartyl protease activity (col.5, line 54 – col.6, line 35). Thus, a polypeptide that includes a fragment of the ASP2 polypeptide of the Powell et al. reference could contain the active site tripeptides without residue 130, thus meeting the limitations of claim 1.

Also, Applicants' assertions that the difference in the Powell et al. and Vassar et al. amino acid sequences is within the domain defined by the active site and that the Vassar et al. reference does not inherently teach an activity for the Powell et al. protein are inaccurate. According to Applicants' own specification, functional fragments that contain the residues between the active sites may be shortened or lengthened, as long as the active sites are maintained (see p.30). Thus, absent evidence to the contrary,

given that position 130 is not apparently crucial for the claimed proteolytic function and given that the Vassar et al. reference teaches the active site tripeptides of DTG and DSG, it does inherently teach an activity for the Powel et al. reference.

In addition, as stated previously, the Powell et al. patent teaches soluble fragments of the ASP2 polypeptide (col.20, line 25), which are polypeptides that lack the transmembrane domain. Thus, it is irrelevant that the Powell et al. reference does not explicitly recite removing a "transmembrane domain," and the limitations of claim 4 have been met. As stated previously, the patent teaches a heterologous tag (col.9, line 50 – col.10, line 45), thus meeting the limitations of claim 3. Moreover as stated above, claim 19 encompasses an aspartyl protease that comprises "an amino acid sequence which is identical across its length to a sequence in SEQ ID NO: 4," and thus, the protease encompasses as little as two amino acids of SEQ ID NO: 4. Thus, the Powell et al. reference does indeed anticipate claim 19.

Therefore, the rejection of claims 1, 3, 4 and 19 under 35 U.S.C. 102(e) is properly maintained.

## *Conclusion*

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

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Patent Examiner
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12 September 2007

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